

Claims

1. A nucleic acid encoding a cytoplasmic signalling molecule comprising at least two cytoplasmic signalling sequences, wherein at least one cytoplasmic signalling sequence is derived from CD134 or ICOS.
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2. A nucleic acid according to claim 1, wherein at least one cytoplasmic signalling sequence is a primary cytoplasmic signalling sequence.
- 10 3. A nucleic acid according to claim 2 wherein the primary signalling sequence contains an ITAM.
4. A nucleic acid according to claim 3, wherein the primary signalling sequence is derived from TCR ζ , FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD5, CD22, CD79a,
15 CD79b or CD66d.
5. A nucleic acid according to claim 3, wherein the primary signalling sequence contains an ITIM.
- 20 6. A nucleic acid according to claim 1, wherein at least one cytoplasmic signalling sequence is a secondary cytoplasmic signalling sequence.
7. A nucleic acid according to claim 6, wherein the secondary cytoplasmic signalling sequence is derived from CD2, CD4, CD5, CD8 α , CD8 β , CD28,
25 CD137, CD134, ICOS or CD154.
8. A nucleic acid according to any one of claims 2 to 7, which encodes three cytoplasmic signalling sequences.
- 30 9. A nucleic acid according to any one of claims 2 to 7, wherein the first cytoplasmic signalling sequence encoded for in reading frame is derived from CD134 or ICOS.

10. A nucleic acid according to claim 9, which encodes i) a cytoplasmic signalling sequence derived from CD134 followed in reading frame by ii) a cytoplasmic signalling sequence derived from TCR ζ .

5 11. A nucleic acid according to claim 9, which encodes i) a cytoplasmic signalling sequence derived from ICOS followed in reading frame by ii) a cytoplasmic signalling sequence derived from TCR ζ .

10 12. A nucleic acid according to any one of claims 2 to 7, wherein the second cytoplasmic signalling sequence encoded for in reading frame is derived from CD134 or ICOS.

15 13. A nucleic acid according to claim 12, which encodes i) a cytoplasmic signalling domain derived from TCR ζ followed in reading frame by ii) a cytoplasmic signalling domain derived from CD134.

20 14. A nucleic acid according to claim 12, which encodes i) a cytoplasmic signalling domain derived from TCR ζ followed in reading frame by ii) a cytoplasmic signalling domain derived from ICOS.

25 15. A nucleic acid according to claim 8, wherein the first cytoplasmic signalling sequence encoded for in reading frame is derived from CD134 or ICOS or from a secondary cytoplasmic signalling sequence.

30 16. A nucleic acid according to claim 15 which encodes in reading frame i) a cytoplasmic signalling sequence derived from CD28, ii) a cytoplasmic signalling domain derived from TCR ζ , and iii) a cytoplasmic signalling sequence derived from CD134.

30 17. A nucleic acid according to claim 15 which encodes in reading frame i) a cytoplasmic signalling sequence derived from CD28, ii) a cytoplasmic signalling domain derived from TCR ζ , and iii) a cytoplasmic signalling sequence derived from ICOS.

18. A nucleic acid encoding a chimeric receptor protein, which comprises an extracellular ligand-binding domain, a transmembrane domain and a cytoplasmic signalling domain, wherein the cytoplasmic signalling domain is encoded by a nucleic acid according to any one of claims 1 to 17.
19. A nucleic acid encoding a chimeric receptor protein, which comprises an extracellular ligand-binding domain, a transmembrane domain and a cytoplasmic signalling domain, wherein the cytoplasmic signalling domain comprises a single cytoplasmic signalling sequence derived from CD134.
20. A nucleic acid encoding a chimeric receptor protein, which comprises an extracellular ligand-binding domain, a transmembrane domain and a cytoplasmic signalling domain, wherein the cytoplasmic signalling domain comprises a single cytoplasmic signalling sequence derived from ICOS.
21. A nucleic acid according to claims 18 and 20 wherein the extracellular ligand-binding domain is an antibody, or an antigen-binding fragment thereof.
22. A nucleic acid according to claim 21 wherein the antigen binding fragment is a Fab' or scFv.
23. A nucleic acid according to any one of claims 18 to 22, wherein the transmembrane domain is derived from the α , β or ζ chain of the T-cell receptor, CD28, CD3 ϵ , CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, ICOS or CD154.
24. A nucleic acid according to claim 23 wherein the transmembrane domain is derived from CD28.
25. A vector comprising a nucleic acid according to any one of the preceding claims.
26. A host cell containing a nucleic acid according to any one of claims 1 to 24, or a vector according to claim 25.

27. A peptide or polypeptide comprising a cytoplasmic signalling molecule encoded by a nucleic acid according to any one of claims 1 to 17.

5 28. A chimeric receptor protein encoded by a nucleic acid according to any one of claims 18-20.

29. A host cell expressing a peptide or polypeptide according to claim 27 or a chimeric receptor protein, according to claim 28.

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30. A host cell according to claims 26 or 29, which is a resting or senescent T-lymphocyte.

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31. A nucleic acid according to any one of claims 1 to 24, or a vector according to claim 25, for use in therapy.

32. A chimeric receptor protein according to claim 28, for use in therapy.

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33. A composition comprising a peptide or polypeptide according to claim 27, a chimeric receptor protein according to claim 28, a nucleic acid according to any one of claims 1 to 24, or a vector according to claim 25, in conjunction with a pharmaceutically acceptable excipient.

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34. The use of a peptide or polypeptide according to claim 27, a chimeric receptor protein according to claim 28, or a composition according to claim 33, in the manufacture of a medicament for the treatment or prevention of disease in humans or in animals.